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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/918,537	08/22/1997	KOICHI AKASHI	LSJU-64PAT	6190

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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	17

DATE MAILED: 07/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 08/918,537	Applicant(s) AKASHI ET AL.	
	Examin r Q. Janice Li	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 1997* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Notice to Comply* .

DETAILED ACTION

The amendment and response filed 3/17/03 have been entered as Paper #16. Claim 1 has been amended, claims 12-18 have been canceled, and claims 1-11 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and arguments will not be reiterated. The arguments in paper #16 are moot in view of newfound art and new grounds of rejections.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

The specification contains nucleic acid sequences (pages 17, 22-23) that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures. Applicant must provide a paper copy and a computer readable copy of the Sequence Listing and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or

1.821(g) or 1.825(b) or 1.825(d). A full response to this Office action must include a complete response to the requirement for a new Sequence Listing.

Claim Rejections - 35 USC §103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, and 6-10 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Olweus et al* (US 6,555,324), in view of *Galy* (US 5,972,627).

Claims 1-3 and 6 are drawn to a composition comprising mammalian common lymphoid progenitor cells, wherein at least 95% of the cells bear surface markers for c-kit^{lo}, IL-7Rα^{+} and Lin^{-}, and wherein said progenitor cells are capable of giving rise to T, B, and NK cells, wherein the cells are further characterized as Thy-1^{-}, and blast cells; wherein the cells are genetically modified to comprise an exogenous DNA vector. Claims 7-9 are drawn to a method of enrichment for said cell composition, wherein the hematopoietic cells from bone marrow, peripheral blood are used initially for selection.

Olweus et al teach that progenitor cells committed to certain lineages can be identified using markers for CD34+ and CD38+, followed by additional markers for different lineages. For progenitors committed to lymphoid lineage, such marker is IL-7R (column 2, lines 36-61). Although *Olweus et al* do not specifically teach the c-kit and lin markers for these cells, *Galy* teaches that this population of cells are Lin^{-}, Thy-1^{-}, (fig. 1,

middle and right panel), and *C-kit*^{low} (column 16, lines 33-42). *Galy* also teaches that said cells are blast cells (collected at in the lymphoblastoid gate) and could be genetically modified (column 5, lines 27-30, and column 12). Because the gating method of collection, only cells positive for the marker would go to the gate, thus, it would be obvious to obtain a cell population with greater than 95% purity at a certain gate. *Galy* goes on to teach a method for purifying and enriching said cells from hematopoietic cell source such as bone marrow and peripheral blood using antibodies recognizing cell surface markers (paragraph bridging columns 8-9). *Galy* teaches "SELECTION OF THESE PROGENITOR CELLS NEED NOT BE ACHIEVED WITH A MARKER SPECIFIC FOR THE CELLS. BY USING A COMBINATION OF NEGATIVE SELECTION AND POSITIVE SELECTION, ENRICHED CELL POPULATIONS CAN BE ACHIEVED" using various separation methods such as magnetic separation, affinity chromatograph and flow cytometry (column 9). One of the methods is measuring the cells by size, granularity, and propidium iodide exclusion in the live cell gate using FACS (column 20, lines 59-65). *Galy* does not teach using IL-7 receptor alpha for cell sorting.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Olweus et al,* by combining CD34+/CD38+ positive selection with Lineage marker-negative selection as taught by *Galy*, followed by the IL-7R selection for identifying and enrichment of lymphoid progenitor cells with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the method because it provides additional criteria for purification, thus, achieving better enrichment of lymphoid progenitor cells.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

It is noted, that the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). For the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. In re Nilssen, 7 USPQ2d 1500 (Fed. Cir. 1988).

Claims 1-4, and 6-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Olweus et al* (US 6,555,324), and *Galy* (US 5,972,627) as applied to claims 1-3 and 6-10 above, further in view of *Kawamoto et al* (Int Immunol 1997 July;9:1011-1019).

Claims 4 and 11 are drawn to selecting the desired cells by Sca-1^{lo} marker. The combined teachings of *Olweus et al*, and *Galy* fails to teach the particular marker. However, before the effective filing date of the instant application, *Kawamoto et al* teach the Sca-I marker and its association with lineage commitment of hematopoietic stem cells. They teach that Sca-1^{+} population are multipotent or unipotent progenitor cells giving rise to both lymphoid and myeloid cells, whereas Sca-1^{-} population only give rise to one of the T, B, or M cells (abstract). They go on to teach, "COMMITMENT TO THE M LINEAGE BEGINS AT THE SCA-1+ STAGE, WHEREAS COMMITMENT TO THE B LINEAGE OCCURS AFTER LOSING THE SCA-1 ANTIGEN".

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Olweus et al*, and *Galy* by simply including Sca-1 as one of the markers for the enrichment of lymphoid progenitor cells, with a reasonable expectation of success. The ordinary skilled artisan would have

been motivated to modify the method because Sca-1^{lo} could eliminate some of the myeloid progenitor cells (a negative selection process as taught by *Galy*) while permit the lymphoid progenitors remain in the population, thus, achieving better enrichment of lymphoid progenitor cells. Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 1-3, and 5-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Olweus et al* (US 6,555,324), and *Galy* (US 5,972,627) as applied to claims 1-3 and 6-10 above, further in view of *Kincade et al* (Int Immunol 1997 July;9:1011-1019) and *Ballas et al* (J Immunol 1990;145:1039-45).

Claim 5 is drawn to additional markers, $CD43^{lo}$, HSA^{lo}, $CD45^{+}$, and Mel-14^{-}. The combined teachings of *Olweus et al*, and *Galy* teach $CD45^{+}$, but fails to teach $CD43^{lo}$, HSA^{lo}, and Mel-14^{-}. However, before the effective filing date of the instant application, *Kincade et al* teach selective regulation of B lymphocyte precursor (lymphoid progenitor) cells by targeting CD45RA, CD43, IL-7, and heat stable antigen (HSA, column 10, lines 3-9). *Ballas et al* teach that thymocytes are MEL-14^{-}, whereas mature peripheral NK cells are MEL-14^{+}.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Olweus et al*, and *Galy* by simply including $CD43^{lo}$, HSA^{lo}, and Mel-14^{-} as markers for the enrichment of lymphoid progenitor cells, with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to do so because additional markers serve to verifying

whether the selected cell population is enriched of lymphoid progenitor cells or contaminated with mature lymphocytes. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

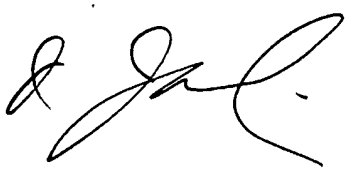
- No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).



Q. Janice Li
Examiner
Art Unit 1632

QJL
June 30, 2003

Notice to Comply	Application No.	Applicant(s)	
	08918537	Weissman et al	
	Examiner	Art Unit	
	Q. Janice Li	1632	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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